

Intensive care unit acquired muscle weakness in COVID-19 patients

Nathalie Van Aerde, MD¹; Greet Van den Berghe*, MD, PhD^{1,3}; Alexander Wilmer*, MD, PhD²; Rik Gosselink*, PT, PhD⁴; Greet Hermans*, MD, PhD^{1,2};

COVID-19 consortium:

Philippe Meersseman, MD²; Jan Gunst MD, PhD^{1,3}; Vicky Aerts, PT, MSc⁴; Tim Balthazar, MD⁵; Astrid Barbé, MD⁶; Arne Böhrer, PT, MSc^{4,8}; Kim Caluwé, PT, MSc^{4,8}; Michael P. Casaer, MD, PhD^{1,3}; Iris Coosemans, PT, MSc^{4,8}; Steve Coppens⁶, MD; Dieter Dauwe, MD, PhD^{1,3}; Yves Debaveye, MD, PhD^{1,3}; Johan De Coster, MD⁶; Paul De Munter, MD⁷, PhD; Lot Demuyndt, PT, MSc^{4,8}; Veerle De Sloovere; MD⁶; Lars Desmet, MD³; Erwin De Troy, MD³; Greet De Vlioger, MD, PhD^{1,3}; Bregje Frickx, PT, MSc^{4,8}; Eline Haghedooren, PT^{4,8}, MSc; Renata Haghedooren, MD³; Liesbet Henckaerts, MD, PhD⁷; Arne Heyns, MD⁸; Miek Hornikx, PT, PhD^{4,8}; Catherine Ingels, MD, PhD^{1,3}; Bart Jacobs, MD³; Kristel Janssen, PT, MSc^{4,8}; Wouter Meersseman, MD, PhD²; Geert Meyfroidt, MD, PhD^{1,3}; Jan Muller, MD³; Arne Neyrinck, MD, PhD⁶; Marijke Peetermans, MD, PhD²; Steffen Rex, MD, PhD⁶; An Schrijvers MD⁶; Peter Vanbrabant, MD⁷; Christophe Vandenbrielle⁵, MD, PhD; Raf Van den Eynde, MD⁶; Marleen van den Hauwe, PT, MSc^{4,8}; Marc Van de Velde, MD, PhD, EDRA⁶; Marine Van Hollebeke, PT, MSc⁴; Eric Van Wijngaerden, MD, PhD⁷; Sandra Verelst, MD, PhD⁹; Dirk Vlasselaers MD, PhD^{1,3}; Claudia Volker, PT, MSc^{4,8}; Bart Vrijisen, PT, PhD^{4,8}; Joost Wauters, MD, PhD²; Pieter J. Wouters, MSc^{1,3};

1 Department of Cellular and Molecular Medicine, KU Leuven, Herestraat 49, B-3000 Leuven, Belgium;

2 Medical Intensive Care Unit, Department of General Internal Medicine, University Hospitals Leuven, Herestraat 49, B-3000 Leuven, Belgium;

3 Department of Intensive Care Medicine, University Hospitals Leuven, Herestraat 49, B-3000 Leuven, Belgium;

4 Department of Rehabilitation Sciences, KU Leuven, Herestraat 49, B-3000 Leuven, Belgium;

5 Department of Cardiovascular Diseases, University Hospitals Leuven, Herestraat 49, B-3000 Leuven, Belgium;

6 Department of Anaesthesiology, University Hospitals Leuven, Herestraat 49, B-3000 Leuven, Belgium;

7 Department of General Internal Medicine, University Hospitals Leuven, Herestraat 49, B-3000 Leuven, Belgium

8 Department of Physical and Rehabilitation Medicine, University Hospitals Leuven, Herestraat 49, B-3000 Leuven, Belgium

9 Department of Emergency Medicine, University Hospitals Leuven, Herestraat 49, B-3000 Leuven, Belgium

*Equally contributed

Corresponding author:

Greet Hermans, MD, PhD, Medical Intensive Care Unit, Department of General Internal Medicine, UZ Leuven, Herestraat 49, B-3000 Leuven, Belgium Tel: +32-16-344275, Fax: +32-16-344230, Email: greet.hermans@uzleuven.be, ORCID: 0000-0001-5340-1500

Dear Editor,

Infection with the SARS-CoV-2 virus may lead to hypoxemic respiratory failure and acute respiratory distress syndrome (ARDS). ARDS is frequently complicated by intensive care unit acquired weakness (ICUAW)(1), which is associated with poor outcomes(2). Critically ill COVID-19 patients may differ from typical ARDS-patients in baseline factors(3) and ICU exposures associated with ICUAW(4). Of particular concern may be the need for deep sedation to avoid patient-ventilator dyssynchrony and ventilator-induced/self-inflicted lung-injury because of high respiratory drive(5). We aimed to assess the incidence of ICUAW in critically ill COVID-19 patients, to identify factors associated with its occurrence, and to describe its short-term outcomes.

This single-center, retrospective, observational study involved adult critically ill COVID-19 patients admitted to the University Hospitals Leuven, from March 13th until June 8th 2020. After April 1st, physiotherapists were re-engaged in patient care and performed daily strength-assessment when appropriate. Records of eligible patients were searched for baseline characteristics, ICU-exposures and outcomes. The primary outcome was the incidence of ICUAW, assessed with the MRC-sum-score(2), at awakening, at ICU- and hospital discharge in patients requiring invasive mechanical ventilation (IMV). Additionally, we evaluated factors and short-term outcomes associated with weakness at ICU discharge. To assess bias, we compared characteristics and outcomes for patients with and without MRC-sum-score, and studied patients without IMV.

Of 486 hospitalized COVID-19 patients, 114 required intensive care of whom 74(64.9%) needed IMV (Supplemental Figure1). Admission and ICU-characteristics are provided in the Online Supplement. Total hospital mortality was 60/486(12.3%), ICU mortality was 11/114(9.6%). All deaths occurred in IMV patients [11/74(14.9%)]. In 50/74(67.6%) assessed IMV patients, the incidences of ICUAW at awakening, ICU- and hospital discharge were 72.0%, 52.0% and 27.0% (Figure1). Those without MRC-sum-score were older as compared to those with MRC-sum-score [67(60-76) versus 60(53-67),p=0.044] and comprised 9 patients who died before awakening, possibly introducing selection bias. Admission characteristics were similar between patients with and without ICUAW, but weak patients

had prolonged ventilation(days) [24(15-29) versus 12(8-17), $p<0.001$], higher mean morning glycemia(mg/dl) [126(119-134) versus 118(110-129), $p=0.041$], and more frequently received dialysis [11/26(42.3%) versus 4/24(16.7%), $p=0.048$]. Exposure to corticosteroids, sedatives and analgesics, except for dexmedetomidine, and NMBAs was higher (see Online Supplement). Weak patients had longer ICU stays(days) [30(19-42) versus 19(12-25), $p=0.008$], lower mobility score at ICU discharge [2(2-2) versus 6(4-6), $p<0.001$], but ICU readmission [0/26(0%) versus 2/24(8.3%), $p=0.225$] and mortality [2/26(7.7%) versus 0/24(0%), $p=0.491$] were not different. Handgrip-strength(%pred) [43%(28%-59%) versus 64%(36%-80%), $p=0.045$], and Barthel at hospital discharge [8(2.5-11.5) versus 10.5(8-18), $p=0.040$], remained lower in weak patients (Figure 1). 15/26(57.7%) weak versus 6/24(25.0%) not-weak patients were referred for in-patient rehabilitation. In 6/40(15.0%) assessed non-IMV patients, 1 patient was weak at ICU discharge and none at hospital discharge. (see Online Supplement).

In conclusion, in this cohort of critically ill COVID-19 patients, survival was high, but those needing prolonged sedation frequently presented with ICUAW. Although strength improved throughout hospitalization, impact on functional status remained substantial. These data indicate that there may be a price to pay for allowing rigorous lung-protective ventilation and underscore the need for follow-up of post-ICU COVID-19 patients, to offer tailored rehabilitation, hopefully reducing long-term impact.

FIGURES

Figure 1. Strength and functional outcomes in COVID-19 patients, requiring invasive mechanical ventilation, with and without weakness at ICU discharge. Panel A: Incidence of ICUAW at awakening, ICU discharge and hospital discharge. Panel B: MRC-sum-score at awakening, ICU discharge and hospital discharge. Panel C: ICU mobility score at ICU discharge. Panel D: Barthel score at hospital discharge.

Abbreviations: *MRC*: Medical Research Council; *ICUAW*: intensive care unit acquired weakness; *ICU*: intensive care unit; *HOS*: hospitalization

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